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CASE REPORT

Delay in diagnosis of hypopituitarism after traumatic head injury: A case report and review of the literature

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Abstract

Neuroendocrine complications are among important and frequently missed complications of traumatic brain injury. Hypopituitarism, the partial or complete insufficiency of anterior pituitary secretion may be underrecognized due to its subtle clinical manifestations in traumatic patients. We report a case of 14½-year-old girl who was admitted due to growth failure and had been diagnosed to have multiple hypophyseal hormone deficiency including thyroid-stimulating hormone, gonadotropins, adrenocorticotropin hormone which developed years after traumatic head injury.

Introduction

The pituitary gland is only 0.5 ml in volume but plays a major role in the endocrine system linking the endocrine system and the central nervous system (CNS). The gland has 2 parts, anterior pituitary (adenohypophysis) and posterior pituitary (neurohypophysis). Hormones secreted by the anterior pituitary are thyrotropin, or thyroid-stimulating hormone (TSH), gonadotropins, or follicle-stimulating hormone (FSH) and luteinizing hormone (LH), growth hormone (GH), corticotrophin, or adrenocorticotropin hormone (ACTH), and prolactin hormone (PRL). Hypopituitarism is defined as partial or complete insufficiency of anterior pituitary secretion [1]. Although trauma is one of leading causes of hypopituitarism, the diagnosis and treatment of hypopituitarism is generally not considered as a high priority after traumatic brain injuries [2]. The diseases caused by hormonal abnormalities related to the posterior pituitary gland such as syndrome of inappropriate secretion of antidiuretic hormone and diabetes insipidus are more commonly concerned but chronic neuroendocrine deficits among patients with traumatic brain injury (TBI) are not considered important [2]. Underdiagnosis or delayed diagnosis of neuroendocrine problems in patients with TBI diminishes the quality of life and may cause serious health problems [1,2].

Case Report

A 14½-year-old girl was admitted to our hospital for growth failure. Parents emphasized that her development had been normal until she had a serious motor-vehicle accident; fallen from tractor when she was nine years old. She had been hospitalized at local state hospital for a week and discharged without any complication. She had no history of operation, intracranial bleeding and had no sequela. However she had failure to thrive after

accident. Her school performance was average. She had no menses and puberty was delayed. At physical examination height was 134 centimeters and weight was 31 kilograms; both were under third percentile. A two centimeters diametered rough scar was present at left forebrain. None secondary sex characters had developed, Tanner stage was I for both mamillary and pubic hair development. No neurologic deficit was observed. The calendar age was 14 ½ years, whereas height and bone ages were 9.5 and 10 years, respectively. Arm span was 135 cm, pubic-heel distance was 66 cm and the height velocity calculated for the last six months was only 1 cm/year. Serum concentrations of all anterior pituitary and related hormones were below normal limits (Table I). Hypophyseal MRI, at T1 weighed coronal and sagital; after injection of contrast media T1 weighed coronal and T2 weighed axial cross sections were obtained. Pituitary gland was fairly slimmed and located posteriorly at sella turcica. Posterior hypophysis was normal. These findings of MRI were consistent with partial empty sella syndrome. Replacement therapy of thyroid hormone; levothyroxine 75 mcg/day p.o., and cortisol; hydrocortisone 20 mg/day p.o. was started. After maintaining euthyroid state; human growth hormone stimulation tests with L-dopa and glucagon-propranolol showed that peak GH concentration was less than 1 ng/ml. Patient was accepted as complete growth hormone deficiency and unresponsive to GH stimulation tests according to guidelines published by American association of clinical endocrinologists [3]. The growth hormone replacement therapy is planned.

Table 1: Hormone profile at admission

Hormones	Measured levels	Normal levels
Thyroid-stimulating hormone	5,6 mcg/dl	5–12 mcg/dl
Cortisol	0.032 mIU/ml	2–10 mIU/ml
Follicle-stimulating hormone	0.89 mcg/dl	5–23 mcg/dl
Luteinizing hormone	1.08 mIU/ml	1–9 mIU/ml
Estradiol	0.31 mIU /ml	2–12 mIU/ml
Dehydroepiandrosteron sulphate	0.20 ng/dl	3.4–17ng/dl
Prolactin	2.0 ng/ml	3–24 ng/ml
Insulin like growth factor 1	1.45 ng/ml	3–24 ng/ml
Insulin like growth factor binding protein 3	5.64 ng/ml	2.2–5.9 mg/L

Discussion

Until recently hypopituitarism after TBI has been considered rare. In an article published in 1942, Escamallia and Lisser reported an incidence of only 0.7% with only 4 out of 595 cases manifesting problem [4]. But recent publications show that hypopituitarism due to head trauma is more common than it was thought. In 2001, Lieberman et al performed endocrine evaluations on 70 patients residing in a postacute brain injury program and demonstrated a rate of abnormalities that was quite higher than found by other authors (48/70 or 59%) [5]. Underdiagnosis or delayed diagnosis of neuroendocrine problems may worsen the mortality and morbidity in patients with TBI.

Neurologic deficits are reported to be common in posttraumatic hypopituitarism. Coma and cranial nerve (CN) deficits including blindness and V, VI, and VII CN palsies are among most common neurologic seqeulae [6]. However pituitary failure can occur even in minor head injuries and can be poorly recognized [7]. There are studies which imply that anterior pituitary dysfunction can be diagnosed years after initial insult [6–8]. Our patient had had a serious accident five years before her admission to our hospital. We could not reach any hospital recordings but parents emphasized that growth was failed after second and more serious accident.

A screening protocol may be adopted for selected patients at risk for endocrine problems. While neuroendocrine screening is not advocated in all TBI patients, physicians should be aware of the importance of neuroendocrine dysfunction following TBI [8,9].

Endocrinologic manifestations of hypopituitarism reveal the deficiencies of specific hormones secreted from pituitary gland including hypoadrencorticotropinemia, hypothyroidsm and hypogonadism. Deficiency in corticotropin is characterized by a decrease in adrenal androgens and production of cortisol. Acute loss of adrenal function is a medical emergency and may lead hypotension and death if not treated. Signs and symptoms of corticotropin deficiency include myalgias, arthralgias, fatigue, headache, weight loss, anorexia, nausea, vomiting, abdominal pain, altered mentation or altered consciousness, dry wrinkled skin, decreased axillary and pubic hair, anemia of chronic disease, and impaired gluconeogenesis [1,4]. Our patient has very low serum concentrations of ACTH and cortisol. No axillary or pubic hair was present, a mild anemia and profound fatigue complaint was present. The clinical and laboratory findings were consistent with hypoadrencorticotropinemia.

Secondary hypothyroidism due to decreased TSH exhibits identical symptoms to primary thyroid disease, only less severe. In our patient despite low serum levels of thyroxine, serum TSH was not elevated, even was significantly lower than normal levels, which make us to think the patient as to have secondary hypothyroidism. Signs and symptoms of secondary hypothyroidism include fatigue, weakness, inability to lose weight, recent weight gain, constipation, cold intolerance, altered mental status, impaired memory, and anemia. Physical examination can reveal bradycardia, delayed relaxation of the deep tendon reflexes, and periorbital puffiness [1,5]. In our patient poor school performance, weakness and fatigue was more prominent symptoms which were probably due to secondary thyroid hormones deficiency.

Gonadotrophin deficiency in children leads to absence of menstruation. Diagnosis of hypogonadotrophic hypogonadism is based on measurement of low serum estradiol concentration in presence of normal or low concentrations of LH. However hyperprolactinaenemia must be excluded. The hormone profile of our patient was consistent with hypogonadotrophic

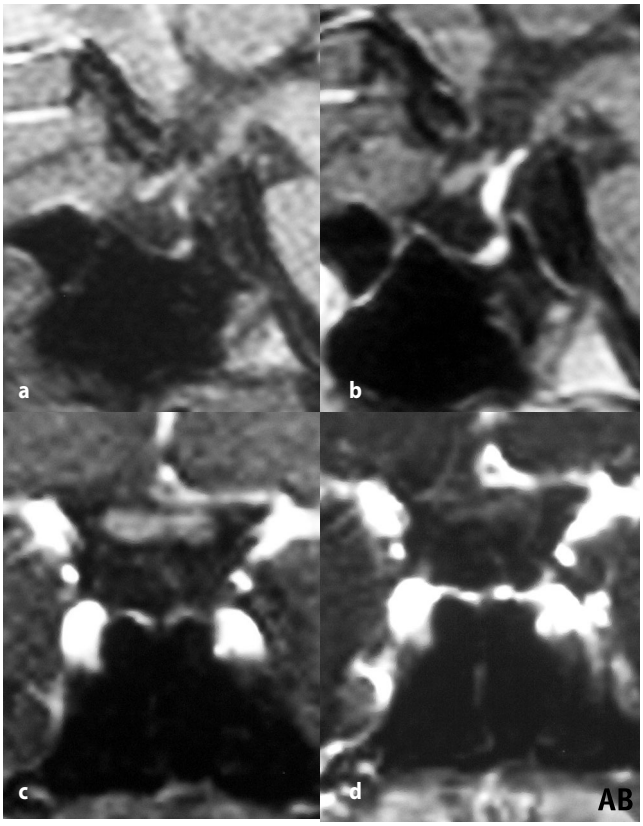

Figure 1: Absence of adenohypophysis at sella tursica
a-b. Unenhanced and enhanced sagittal T1 sequences
c-d. Unenhanced and enhanced coronal T1 sequences

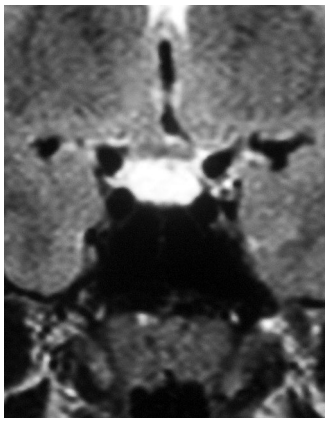

Figure 2: Coronal T2-weighted image show no evidence of anterior pituitary tissue.

hypogonadism. In children, FSH and LH deficiency can cause eunuchoidism and lack of sexual development. Our patient also had no sexual development or menses. Sex hormone replacement therapy is required for these patients for short term relief of symptoms (loss of libido and dyspareunia) and for long term prevention of osteoporosis and atherosclerosis. A combined oral contraceptive containing 20–35 mcg ethiniyl estradiol is an acceptable and often preferred therapy in hypogonadotrophic hypogonadism [10]. We have planned to start of sex hormone replacement therapy after achievement of growth by hormone replacement therapy.

The US Food and Drug Administration (FDA) defines complete growth hormone deficiency by stimulated peak serum GH concentrations <5 ng/ml. In our patient peak GH concentrations following L-dopa and glucagon-propranolol stimulation tests were less than 1 ng/ml. In children, GH deficiency presents as growth retardation and delayed sexual maturation. Our patient had growth failure as well as delayed sexual maturation. Although in GH deficiency patients may present with fasting hypoglycemia due to loss of the gluconeogenic effect of GH, which counteracts the effect of insulin, our patient had no fasting hypoglycemia [1,4,7,8].

In conclusion, in this report we want to emphasize the importance of investigating the endocrine status of patients with TBI. Although patients may appear normal after the injury, we suggest they should have close follow up for possible hypopituitarism and the patients and families should be cautioned against the possible late-onset problems and growth failure. Appropriate and early management of patients with TBI may result in physically and psychologically healthier children.

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